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CURRICULUM VITAE

Name: NON-RESPONSIVE

Date of birth:

Place of birth: NON-RESPONSIVE

Home address:

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Department of Biomedical and
Environmental Health Sciences
313 Warren Hall
School of Public Health
University of California
Berkeley, CA 94720

Business phone: (415)642-8770

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Marital status: Married

Children: One

Nationality: British

Visa status: Permanent Resident

Education:

Oct. 1977 - Sept. 1980

Department of Biochemistry and Chemistry
Medical College of St. Bartholomew's Hospital
Charterhouse Square, London EC1M 6BQ

Ph.D. in Biochemistry

Ph.D. Title: Studies on Oxidative Drug Metabolism using Quantitative Cytochemical and Biochemical Methods.

Supervisor: Professor E.D. Wills
Dept. Head: Professor E.M. Crook

Oct. 1974 - Sept. 1977

Queen Elizabeth College
University of London

B.Sc. (Hons) degree in Biology, (Upper - Second Class)

Specialization in Cell Biology and included a full year of Mathematics, Physics and Chemistry. Third year project completed in the Division of Cellular Biology, Kennedy Institute of Rheumatology, London, under the supervision of Drs. J. Chayen and L. Bitensky.

Employment:

Oct. 1982 - present

Department of Biomedical and Environmental Health Sciences, School of Public Health
University of California
Berkeley, CA 94720

Assistant Professor of Occupational Toxicology

Responsibilities include instruction and supervision of graduate student research in toxicology and the development of an independent research program in toxicology. Co-teaching Environmental Toxicology lecture course and Industrial Toxicolgy laboratory course with Professor Wei.

Sept. 1981 - Sept. 1982

Toxicology Unit of the Department of Pharmacology
The School of Pharmacy
University of London

Teaching Fellow (Junior Lecturer)

Lecturing duties included teaching part of the first combined B.Sc. degree course in Toxicology and Pharmacology offered in the U.K. and giving lectures for the University of London Biochemical Toxicology B.Sc. course unit at the Medical College of St. Bartholomew's Hospital. Dr. G.M. Cohen is the head of the Toxicology Unit and Dr. J.A. Timbrell also lectures on the above course.

Sept. 1980 - Sept. 1981

Department of Forensic Medicine
Karolinska Institute
Stockholm, Sweden

Post-doctoral research

Guest research scientist in collaboration with Professor Sten Orrenius and his research team which led to a number of important findings and publications in the field of biochemical toxicology. This collaboration still continues.

Professional References:

1) Professor S. Orrenius, Department of Forensic Medicine, Karolinska Institutet, S-104 01 Stockholm 60, Sweden

2) Professor E.D. Wills, The Medical College of St. Bartholomew's Hospital, Charterhouse Square, London EC1M 6BQ, United Kingdom.

3) Professor B.N. Ames, Biochemistry Dept., University of California, Berkeley, California 94720.

4) Dr. G.M. Cohen, Toxicology Unit, The School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX, United Kingdom.

Society Memberships

Society of Toxicology
Society for Free Radical Research
Genetic and Environmental Toxicology Association
Northern California Cancer Program

Published Research Papers (*Indicates Refereed Publications)

1) Smith, M.T. (1978) Effects of Chronic Low Doses of L-Thyroxine on Succinate Dehydrogenase Activity in the Mammalian Liver and Myocardium. Biochem. Soc. Trans. 6:131-133.

*2) Smith, M.T., Darmon, J., Wills, E.D. and Dondi, P.G. (1979) Rapid Data Analysis in Quantitative Cytochemistry. Histochem. J. 11:370-371.

*3) Smith, M.T., Loveridge, N., Wills, E.D. and Chayen, J. (1979) The Distribution of Glutathione in the Rat Liver Lobule. Biochem. J. 182:103-108.

4) Smith, M.T., and Wills, E.D. (1980) Studies on the Validity of the Acid Haematein Method for the Investigation of the Fatty Acid Composition of Liver Phospholipids. Proc. Roy. Micro. Soc. 15:111-112.

5) Smith, M.T. and Wills, E.D. (1980) A Comparison of Biochemical and Cytochemical Methods for Studying the Utilization of NADPH in Rat Liver. Proc. Roy. Micro. Soc. 15:114-115.

*6) Smith, M.T., Wills, E.D., Drew, K., Maxwell, C., Daly, J.R., Reader, S.C.J. and Robertson, W.R. (1980) Applications of an Inexpensive, General Purpose Microcomputer in Quantitative Cytochemistry. Histochem. J. 68:321-323.

*7) Smith, M.T., and Wills, E.D. (1981) Effects of Dietary Lipid and Phenobaritone on the Distribution and Concentration of Cytochrome

P-450 in the Liver studied by Quantitative Cytochemistry. FEBS Letts. 127:33-36.

*8) Smith, M.T. and Wills, E.D. (1981) Effect of Dietary Lipid and Phenobarbitone on the Production and Utilization of NADPH in the Liver. A Combined Biochemical and Quantitative Cytochemical Study. Biochem. J. 200:691-699.

*9) Henderson, B., Loveridge, N., Robertson, W.R. and Smith, M.T. (1981) The Influence of the Storage of Tissue Blocks at -70° C on Enzyme Activity: A Quantitative Cytochemical Study. Histochemistry 72:545-550.

*10) Smith, M.T., Thor, H. and Orrenius, S. (1981) Toxic Injury to Isolated Hepatocytes is Not Dependent on Extracellular Calcium. Science 213:1257-1259.

*11) Smith, M.T., Thor, H., Hartzell, P. and Orrenius, S. (1982) The Measurement of Lipid Peroxidation in Isolated Hepatocytes. Biochem. Pharmacol. 31:19-26.

*12) Jewell, S.A., Bellomo, G. Thor, H., Orrenius, S. and Smith, M.T. (1982) Bleb Formation in Hepatocytes during Drug Metabolism is Caused by Disturbances in Thiol and Calcium Ion Homeostasis. G., Science 217:1257-1259.

*13) Thor, H., Smith, M.T., Hartzell, P., Bellomo, G., Jewell, S.A. and Orrenius, S. (1982) The Metabolism of Menadione in Isolated Hepatocytes. A Study of the Implications of Oxidative Stress in Intact Cells. J. Biol. Chem., 257:12419-12425.

*14) Smith, M.T., Thor, H., and Orrenius, S. (1983) Role of Lipid Peroxidation in the Toxicity of Foreign Compounds to Liver Cells. Biochem. Pharmacol. 32:763-764.

*15) Jones, D.P., Thor, H., Smith, M.T., Jewell S.A. and Orrenius, S. (1983) Inhibition of ATP-Dependent Microsomal Ca^{2+} Sequestration during Oxidative Stress and Its Prevention by Glutathione. J. Biol. Chem., 258:6390-6393.

*16) Cohen, G.M., Wilson, G.D., Gibby, E.M., Smith, M.T., Doherty, M.D., and Connors, T. (1983) 1-Naphthol: A Potential Anti-cancer Agent. Biochem. Pharmacol., 32:2363-2365.

*17) Smith, M.T., Redick, J.A. and Baron, J. (1983) Quantitative Immunocytochemistry: A Comparison of Microdensitometric Measurement of Unlabeled Antibody Peroxidase-antiperoxidase Staining and of Microfluorometric Measurement of Indirect Fluorescent Antibody Staining for NADPH-cytochrome c (P-450) Reductase. J. Histochem. Cytochem., 31:1183-1189.

18) Smith, M.T. and Orrenius, S. (1984) Studies on Drug Metabolism and Drug Toxicity in Isolated Mammalian Cells, In: Drug Metabolism and

Drug Toxicity, (Horning, M.D. and Mitchell, J.R., eds.), pp. 71-98, Raven Press, N.Y.

*19) Smith, M.T., Thor, H. and Orrenius, S. (1984) Detection and Measurement of Drug-Induced Oxygen Radical Formation in "Oxygen Radicals in Biological Systems", Meths. Enzymol. (Packer, L., ed), Vol. 105, pp. 505-510, Academic Press, New York.

*20) de Peyster, A., Quintanilha, A., Packer, L. and Smith, M.T. (1984) Oxygen Radical Formation Induced by Gossypol in Rat Liver Microsomes and Human Sperm. Biochem. Biophys. Res. Commun., 118:573-579.

*21) Doherty, M.D., Cohen, G.M. and Smith,M.T. (1984) Mechanisms of Toxicity of 1-Napthol to Isolated Hepatocytes. Biochem. Pharmacol., 33:543-549.

*22) Thornalley, P.J., Doherty, M.D, Smith, M.T., Bannister, J.M. and Cohen, G.M. (1984) Production of Active Oxygen Species during the Metabolism of 1-Naphthol in vitro. Chem.-Biol. Interact., 48:195-206.

23) Chesis, P.L., Levin, D.B., Smith, M.T., Ernster, L. and Ames, B.N. (1984) Quinone Mutagenicity: Pathways of Metabolic Activation and Detoxification. Proc. Natl. Acad. Sci. USA, 81:1696-1700.

24) Smith, M.T. and Evans, C.G. (1984) Inhibitory Effect of Superoxide-Generating Quinones on Superoxide Dismutase. Biochem. Pharmacol. 33:3109-3110.

Papers Presented at Professional Meetings

(a) Invited

1) Smith, M.T., Thor, H. and Orrenius, S. (1982) The Formation and Inactivation of Active Oxygen Species during Drug Metabolism in Isolated Hepatocytes, In: Microsomes, Drug Oxidations and Drug Toxicity: (Sato, R. and Kato, R., eds.), Japan Sci. Soc. Press, Tokyo, pp. 605-612.

2) Orrenius, S., Jewell, S.A., Thor, H., Bellomo, G., Eklow, L. and Smith, M.T. (1983) Drug-Induced Alterations in the Surface Morphology of Isolated Hepatocytes, In: Isolation, Characterization and Use of Hepatocytes. (Harris, R.A. and Cornell, N.W., eds.) pp. 333-340, Elsevier, Amsterdam.

3) Orrenius, S., Jewell, S.A., Bellomo, G., Thor, H., Jones, D.P. and Smith, M.T. (1983) The Regulation of Calcium Compartmentation in the Hepatocyte - A Critical Role of Glutathione In: "Glutathione: Biochemical, Physiological, Toxicological and Clinical Aspects," (Larsson, A. et al., eds.), Raven Press, pp. 261-271, N.Y.

4) Smith, M.T., Sandy, M.S., Thor, H. and Orrenius, S. (1984) Free-Radical-Induced Changes in the Surface Morphology of Isolated

Hepatocytes, In: "Free Radicals in Molecular Biology and Aging," (Armstrong, D. et al., eds.), Ch. 10, Raven Press, N.Y.

5) Bellomo, G., Jewell, S.A., Smith, M.T., Thor, H. and Orrenius, S. (1984) Perturbation of Ca^{2+} Homeostasis During Hepatocyte Injury, In: Mechanisms of Hepatocyte Injury and Death (Keppler, D., Popper, H., Bianchi, L. and Reutter, W., eds.), p.119-128, MTP Press, Boston.

6) Smith, M.T. (1984) Role of Oxygen Radicals in the Mutagenic, Carcinogenic and Anticancer Properties of Quinones, In: "Free Radicals in Chemistry and Biology," (Bannister, J. et al, eds.), Life Chemistry Reports, in press.

7) Orrenius, S., Thor, H., Dimonte, D., Bellomo, G., Nicotera, P., Ross, D. and Smith, M.T. (1984) Mechanisms of Oxidative Cell Injury Studied in Intact Cells, In: Microsomes and Drug Oxidations, 6th Int. Symp., (Davis, D.D. et al., eds.) Taylor and Francis, U.K., in press.

(b) Submitted

1) Smith, M.T. and Wills, E.D. (1982) Mechanism of Phenobarbitone Potentiation of Centrilobular Hepatic Necrosis In: "Biological Reactive Intermediates," Vol. 2 (Snyder, R., Parke, D.V., Kocsis, J.J., Jollow, D.J., Gibson, G.G. and Witmer, C.M., eds.), Plenum Press, New York, pp. 463-470.

2) Thor, H., Smith, M.T., Hartzell, P. and Orrenius, S. (1982) Toxic and Nontoxic Pathways during Metabolism of Menadione (2-Methyl-1,4-Naphthoquinone) in Isolated Hepatocytes In: "Cytochrome P-450, Biochemistry, Biophysics and Environmental Implications," (Hietanen, E., Laitinen, M. and Hanninen, O., eds.), Elsevier, Amsterdam, pp. 729-732.

3) Smith, M.T., Doherty, M.D., Timbrell, J.A. and Cohen, G.M. (1982) Studies on the Metabolism and Toxicity of 1-Naphthol in Isolated Hepatocytes In: "Cytochrome P-450: Biochemistry, Biophysics and Environmental Implications," (Hietanen, E., Laitinen, M. and Hanninen, O., eds.), Elsevier, Amsterdam, pp. 725-728.

4) Smith, M.T., Fluck, D.S., Eastmond, D.A. and Rappaport, S.M. (1984) Detection of Quinone Metabolites by HPLC with Reductive Electrochemical Detection, In: "Free Radicals in Chemistry and Biology," (Bannister, J. et al, eds.), Life Chemistry Reports, in press.

Papers in Press

1) Smith, M.T., Evans, C.G., Thor, H. and Orrenius, S. (1984) Quinone-Induced Oxidative Injury to Cells and Tissues, In: "Oxidative Stress," (Sies, H., ed.), Academic Press, N.Y., in press.

2) Fluck, D.S., Rappaport S.M. and Smith, M.T. (1984) Conversion of 1-Naphthol to Naphthoquinone Metabolites by Rat Liver Microsomes: Demonstration by High Pressure Liquid Chromatography with Electrochemical Detection. Arch. Biochem. Biophys., in press.

3) Bleeke, M.S., Smith, M.T. and Casida, J.E. (1984) Metabolism and Toxicity of Metribuzin in Mouse Liver. Pesticide Biochem. Physiol., in press.

Manuscripts Submitted or in Preparation

1) de Peyster, A., Sandy, M.S. and Smith, M.T. (1984) Mechanisms Involved in the Acute Toxicity of Gossypol to Isolated Hepatocytes. Toxicol. Appl. Pharmacol., submitted.

2) Smith, M.T. and Sandy, M.S. (1984) Role of Extracellular Ca^{2+} in Toxic Liver Injury: Comparative Studies with the Perfused Liver and Isolated Hepatocytes. Toxicol. Appl. Pharmacol., submitted.

3) Talcott, R.E., Smith, M.T. and Giannini, D.D. (1984) Inhibition of Microsomal Lipid Peroxidation by Naphthoquinones: Structure-Activity Relationships and Possible Mechanisms of Action. Arch. Biochem. Biophys., submitted.

4) Svensson, S.A., and Smith, M.T. (1984) Quantitation of Cytochrome P-450 by Computer-based Second Derivative Spectroscopy, Analyt. Biochem., in preparation.

Meeting Abstracts

1) Wills, E.D. and Smith,M.T. (1979) Evaluation of Quantitative Cytochemical Methods for the Measurement of Oxidative Drug and Carcinogen Metabolism. Abstr. XIth Int. Cong. Biochem., Toronto, Canada, July, 1979, p. 694.

2) Smith, M.T., Loveridge, N., Wills, E.D. and Chayen, J. (1979) The Distribution of Glutathione and its Relationship to the Toxicity of Foreign Compounds in the Liver. Abstr. XIth Int. Cong. Biochem., Toronto, Canada, July 1979, p. 689.

3) Smith, M.T. and Wills, E.D. (1980) The Effect of Dietary Lipid on the Distribution of Cytochrome P-450 in Rat Liver. Abstr. VIth Int. Congr. Histochem., Brighton, United Kingdom, p. 200.

4) Smith, M.T., Lewis, G.M. and Wills, E.D. (1980) The Distribution of Cytochrome P-450 Peroxidase Activity in Rat Liver. Abstr. VIth Int. Congr. Histochem., Brighton, U.K., p. 201.

5) de Peyster, A. and Smith, M.T. (1983) Gossypol, A Proposed Male Contraceptive, is Highly Toxic to Isolated Hepatocytes. 44th Annual O.S.U. Biology Colloquium "Mechanisms of Cellular Toxicology", Corvallis, OR.

6) Sandy, M., Noel, M. and Smith, M.T. (1983) The Role of Extracellular Calcium in Toxic Liver Injury. 44th Annual O.S.U. Biology Colloquium, "Mechanisms of Cellular Toxicology", Corvallis, OR.

7) Smith, M.T. (1984) Quinones as Carcinogens and Anticarcinogens. Society for Free Radical Research, 2nd Annual Meeting, York, U.K..

8) Smith, M.T., Fluck, D.S., Eastmond, D.A. and Rappaport, S.M. (1984) Detection of Quinone Metabolites by HPLC with Reductive Electrochemical Detection. Society for Free Radical Research, 2nd Annual Meeting, York, U.K..

9) Evans, C.G. and Smith, M.T. (1984) Inhibition of Superoxide Dismutase by Superoxide-Generating Quinones. Society for Free Radical Research 2nd Annual Meeting, York, U.K..

10) Smith, M.T., Fluck, D.S., Eastmond, D.A. and Rappaport, S.M. (1984) Detection of Quinone Metabolites by HPLC with Reductive Electrochemical Detection. IUPHAR 9th Int. Congr. of Pharmacol., London, Abstract 127P.

11) Evans, C.G. and Smith, M.T. (1984) Inhibition of Superoxide Dismutase by Superoxide-Generating Quinones. IUPHAR 9th Int. Congr. of Pharmacol., London, Abstract 128P.

12) Smith, M.T. and Wirt, H.J.C. (1984) Quantitative Distribution of DT-Diaphorase Activity in Rat Kidney. 2nd Int. Symp. on Nephrotoxicity, Guildford, U.K.

List of Funded Research Grants on which I am/was P.I. or co-P.I. (Direct costs are given)

1) University-wide Energy Research Group, $12,800 (with Professor E.T. Wei), 3/1/83 - 2/28/84, "Toxicity of Nitroaromatic Compounds Adsorbed on Carbonaceous Particles."

2) Cancer Research Coordinating Committee, University of California, $17,000, 7/1/83 - 6/30/84, "Development of New Selective Anticancer Agents Using Human Organ Culture as the Model Test System."

3) Committee on Research, University of California, $10,000, 7/1/83 - 6/30/84, Purchase of a Vickers M85 Microdensitometer.

4) Biomedical Research Support Program, N.I.H., $5,000, 6/2/83, Purchase of a Vickers M85 Microdensitometer.

5) Faculty Development Program, University of California, Summer Research Grant, $2,890, "Studies on the Role of Calcium in Halogenated Solvent Hepatotoxicity."

6) Sandy, M., Noel, M. and Smith, M.T. (1983) The Role of Extracellular Calcium in Toxic Liver Injury. 44th Annual O.S.U. Biology Colloquium, "Mechanisms of Cellular Toxicology", Corvallis, OR.

7) Smith, M.T. (1984) Quinones as Carcinogens and Anticarcinogens. Society for Free Radical Research, 2nd Annual Meeting, York, U.K..

8) Smith, M.T., Fluck, D.S., Eastmond, D.A. and Rappaport, S.M. (1984) Detection of Quinone Metabolites by HPLC with Reductive Electrochemical Detection. Society for Free Radical Research, 2nd Annual Meeting, York, U.K..

9) Evans, C.G. and Smith, M.T. (1984) Inhibition of Superoxide Dismutase by Superoxide-Generating Quinones. Society for Free Radical Research 2nd Annual Meeting, York, U.K..

10) Smith, M.T., Fluck, D.S., Eastmond, D.A. and Rappaport, S.M. (1984) Detection of Quinone Metabolites by HPLC with Reductive Electrochemical Detection. IUPHAR 9th Int. Congr. of Pharmacol., London, Abstract 127P.

11) Evans, C.G. and Smith, M.T. (1984) Inhibition of Superoxide Dismutase by Superoxide-Generating Quinones. IUPHAR 9th Int. Congr. of Pharmacol., London, Abstract 128P.

12) Smith, M.T. and Wirt, H.J.C. (1984) Quantitative Distribution of DT-Diaphorase Activity in Rat Kidney. 2nd Int. Symp. on Nephrotoxicity, Guildford, U.K.

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5) Faculty Development Program, University of California, Summer Research Grant, $2,890, "Studies on the Role of Calcium in Halogenated Solvent Hepatotoxicity."

6) Committee on Research, Faculty Research Grant, $950, 1983-84, "Development of Quantitative Cytochemical Techniques for Studies on Lung Toxicology."

7) National Foundation for Cancer Research, $440,000 (with Professor L. Packer, Physiology-Anatomy and Professor B. Ames, Biochemistry), 10/1/83 - 9/30/85, "Free Radical Generation and Protection in Membranes: Developing a Strategy for Targeting of Cancer."

8) NCI CA°I3525-12 Project 3C, $60,847, 4/1/84-3/31/85, "Role of Biotransformation in Resistance."

Research Grants Pending

1) N.I.E.H.S., $203,791, 4/1/84 - 3/31/87, "Toxicological Studies using Quantitative Cytochemistry." Approved. Awaiting funding decision.

2) National Foundation for Cancer Research, $300,000, 10/1/85 - 9/30/86, Continued funding of NFCR grant above.

3) NCI, Brain Tumor Research Center, UCSF Program Project Grant, Project 3C, $785,005, 4/1/85 - 3/31/90, "A Biochemical Approach to Targeting Drug Resistant Human Brain Tumor Cells."

4) Pennwalt, 1/1/84 - 12/31/84, $32,680, "The Development of Micromethods for Screening the Efficacy and Toxicity of Potentially Useful New Compounds."

Grants on which I am a Co-Investigator

1) NCI, CA 13525-12 Project 3A, 5% time, "Patterns of Brain Tumor Cell Resistance," 4/1/84 - 3/31/85 funded, 4/1/85 - 3/31/90 pending.

Invited Lectures in 1984

1) January 4, 1984, "Toxic Injury to the Liver, "Dept. of Chemical Pathology, University of Manchester, U.K.

2) January 6, 1984, "Quinones as carcinogens and anticarcinogens," Central Toxicology Laboratory, I.C.I. (U.K.) plc, Macclesfield, U.K..

3) January 9, 1984, "Quinones as carcinogens and anticarcinogens," Dept. of Biochemistry, Brunel University, Uxbridge, U.K..

4) January 10, 1984, "Quinones as carcinogens and anticarcinogens," School of Pharmacy, London, U.K..

5) February 24, 1984, "Drugs that generate oxygen radicals," Workshop on Biomedical Implications of Oxygen Toxicity which I co-organized.

6) Committee on Research, Faculty Research Grant, $950, 1983-84, "Development of Quantitative Cytochemical Techniques for Studies on Lung Toxicology."

7) National Foundation for Cancer Research, $440,000 (with Professor L. Packer, Physiology-Anatomy and Professor B. Ames, Biochemistry), 10/1/83 - 9/30/85, "Free Radical Generation and Protection in Membranes: Developing a Strategy for Targeting of Cancer."

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4) Pennwalt, 1/1/84 - 12/31/84, $32,680, "The Development of Micromethods for Screening the Efficacy and Toxicity of Potentially Useful New Compounds."

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2) January 6, 1984, "Quinones as carcinogens and anticarcinogens," Central Toxicology Laboratory, I.C.I. (U.K.) plc, Macclesfield, U.K..

3) January 9, 1984, "Quinones as carcinogens and anticarcinogens," Dept. of Biochemistry, Brunel University, Uxbridge, U.K..

4) January 10, 1984, "Quinones as carcinogens and anticarcinogens," School of Pharmacy, London, U.K..

5) February 24, 1984, "Drugs that generate oxygen radicals," Workshop on Biomedical Implications of Oxygen Toxicity which I co-organized.

6) March 16, 1984, "Quinones, oxygen radicals and cancer," Dept. of Physiology-Anatomy, U.C., Berkeley, organized by Professor Timiras.

7) May 14, 1984, "Quinones as carcinogens and anticarcinogens," Wayne State University, Dept. of Chemistry, Detroit. Organized by Professor L. Marnett.

8) May 24, 1984, "Free-radical toxicology," NCOHC Grand Rounds organized by Charles Becker, M.D.

9) May 31, 1984, "The risk posed by ethylene dibromide in processed foods," Advisory committee to the Governor, Sacramento, California.

10) July 6, 1984, "Role of oxygen radicals in the mutagenic, carcinogenic and anticancer effects of quinones," Plenary lecture at 2nd Ann. Meeting of Society for Free Radical Research, York, U.K..

LITERATURE CITED

Cohen, G.M., Bracken, W.M., Iyer, R.P., Berry, D.L., Selkirk, J.K. and Slaga, T.J. (1979) Cancer Research 39, 4027-4033

Conney, A.H. (1982) Cancer Research 42, 4875-4917.

Doll, R. and Peto, R. (1981) "The Causes of Cancer", Oxford University Press, Oxford and New York.

GESAMP (IMCO/FAO/UNESO/WHO/IAEA/UN Joint Group of Experts on the Scientific Aspects of Marine Pollution) (1977) Impact of oil on the marine environment. Report No. 6, Stud. GESAMP.

Hoffman, D. and Wynder, E.L. (1963) J. Air Pollution 13, 322-327.

Hogan, M.D. and Hoel, D.G. (1982) in "Principles and Methods of Toxicology", (A.W. Hayes, ed.) pp. 711-731, Raven Press, New York.

International Agency for Research on Cancer (IARC) (1973) IARC Monograph 3, pp. 47, 100, 161.

King, P.J. (1977) Rapport et Procedes Verbales 171, 202-211

Miller, E.C., Miller, J.A., Brown, R.R. and MacDonald, J.C. (1958) Cancer Research 18, 469-477.

Neal, J. and Rigdon, R.H, (1967) Texas Reports on Biology and Medicine 25, 553-557.

Richardson, H.L., Stier, A.R. and Borsos-Nachtnebel, E. (1952) Cancer Research 12, 356-361.

Schelde, E., Kuntzman, R., Haber, S. and Conney, A.H. (1970) Cancer Research 30, 2893-2897.

WILLIAM RENFRO HAVENDER (202) 554 - 2243

Curriculum Vitae

October, 1984

Education: University of California, Berkeley, CA, 1961 - 69
Ph.D. in Genetics (specializing in bacteriophage genetics, and including two years of research at the Max Planck Institute for Molecular Genetics in Berlin, from 1967 - 69).

Cornell University, Ithaca, N.Y., 1957 - 61
B.S. in Horticulture (specializing in Plant Physiology and Chemistry).

Scandinavian Seminar, Ry Folkehøjskole, Denmark
1959 - 60 (Junior Year)

Current Occupation: Consultant on environmental carcinogens

Selected List of Consulting Clients:

Calorie Control Council, Atlanta, GA
Carlton Fields, et al, Tampa, FL
City of Burbank, CA
Clairol/Bristol-Myers, New York, NY
Edith Efron, author, Rochester, NY
Proctor & Gamble, Cincinnati, OH
Elizabeth M. Whelan, author, New York, NY
Aaron Wildavsky, author, Berkeley, CA

Research: Co-leader with Dr. Lois Gold of the Carcinogenic Potency project at the Department of Biochemistry, University of California at Berkeley, 1979 - 81 (under the sponsorship of Dr. Bruce Ames).

The near-term aim of this project was to devise a means of quantitatively analyzing animal cancer bioassays so as to abstract a numerical index of the degree of carcinogenic potency manifested by a given chemical. The index chosen, in consultation with Drs. Richard Peto (Oxford University) and Malcolm Pike (University of Southern California Medical School) is the TD_{50} (Tumorogenic Dose-Rate 50). This refers to the daily dose-rate of a substance that under chronic administration will generate cancer in 50% of exposed animals. A large database was assembled containing information from the National Cancer Institute animal cancer bioassay series on some 200 chemicals, and all tests reported in the literature on this same group of chemicals. These data were used to estimate TD_{50}'s for the various chemicals.

The utility of this work is:

a) It will now be possible quantitatively to compare different tests on the same compound, and in particular, to see how well rats and mice agree with one another in carcinogenic potency, and with other species (including, where data permit, mankind). This should provide some insight into how to make interspecies risk extrapolations, particularly from laboratory test animals to humans.

b) It will be possible in some cases to reconcile contradictory results in independent experiments, for example, positive and negative results with the same chemical in the same species. Negative outcomes often result from the use of low doses or small numbers of animals, and our statistical analysis allows us to calculate the degree of "negativeness", i.e., we can set a lower bound on the possible value of the TD_{50}, based on the number of animals at risk, the doses used and the pattern of mortality among the dose groups. Comparison of this bound from the negative test with the value of the TD_{50} in the positive test will reveal those instances where the apparent discrepancy is due merely to the weaker statistical power of the negative test.

c) Calculation of such bounds in negative tests will allow for the first time such negative tests to be used in quantitative risk assessment, in that one can use the TD_{50} bound to calculate a "cap" on the possible carcinogenicity of a substance.

d) The use of the TD_{50} will help policymakers in corporations and government regulatory agencies to set sensible priorities in trying to reduce dangerous human exposures. Our quantitative analyses of animal cancer bioassays establish that chemicals can vary in carcinogenic potency over a range of at least some million-fold. This means that a dose of the most potent carcinogens known (aflatoxin B_1, dioxin) would cause roughly a million times as many cases of cancer as the same dose of the weakest carcinogens known (saccharin, trichloroethylene). Such a vast range in intrinsic hazard must be taken into account in setting the level of exposure standards, in choosing which among numerous hazards to go after first, and in allocating the limited resources available for risk reduction in a sensible, cost-effective manner. It is of course clear that animal tests will not be an uncomplicated guide, even for ranking relative hazards, but one is probably better off taking this information into consideration than by treating all cancer hazards as of equal magnitude.

The long-term goal of this project is to see whether a quantitative correlation can be established between carcinogenic and mutagenic potency, rather than the merely qualitative correlation that exists now. If one could estimate the degree of carcinogenic potency from the degree of mutagenic potency, then the utility of short-term tests (such as the "Ames" test) would be greatly enhanced, since these could now be used for setting initial priorities within a group of mutagenic chemicals.

Memberships, Associations:

American Association for the Advancement of Science
American Council on Science & Health (member, Board of Scientific Advisors, 1979 - present)
Commonwealth Club of San Francisco
Economics Round Table of San Francisco (Program Chairman, 1981 - 82, President, 1982 -83)
Environmental Mutagen Society
Mont Pelerin Society
The Philadelphia Society
Regulation magazine editorial board (Contributing Editor, 1979 - present)
San Francisco Planning and Urban Research Association
Society for Risk Analysis

Languages: German, Danish

Selected Publications - Articles:

Havender, W.R. and T.A. Trautner (1970), "Temperature Sensitive Mutants and the Establishment of a Linkage Map with B. subtilis Phage SP50", Mol. Gen. Gen. 108, pp. 61 - 69.

Havender, W.R. and T.A. Trautner (1972), "Biological Effects of DNA Cleavage and the Physical Basis of the Map of B. subtilis Phage SP50", Mol. Gen. Gen. 116, pp. 51 - 57.

Havender, W.R. (1976), "Sense and Nonsense about the Jensenist Heresy", The Alternative (now called The American Spectator) 9, April, pp. 10 - 13.

Havender, W.R. (1977), "IQ and Equality: On the Jensen Debate", Dissent, Spring, pp. 221 - 223.

Havender, W.R. (1978), "The 'Gauze Curtain' at Harvard Medical School", The American Spectator 11, May, pp. 31 - 34.

Havender, W.R. (1979), "Ruminations on a Rat: Saccharin and Human Risk", Regulation 3, March/April, pp. 17 - 24.

Havender, W.R. (1980), "On Human Hubris", a contribution to a symposium on E.O. Wilson's book, "On Human Nature", Political Psychology 2, No. 1, pp. 52 - 58.

Havender, W.R. (1980), "When Intelligence Passes the Test", The American Spectator 13, June, pp. 12 - 15.

Havender, W.R. (1980), "Regulatory Misuse of Science", ACSH News & Views 1, November/December, pp. 8 - 9.

Havender, W.R. (1980) Contributor to a symposium on Arthur Jensen's book, "Bias in Mental Tests", The Behavioural and Brain Sciences 3, Fall, pp. 345 - 346.

Ames, B.N., K. Hooper, C.B. Sawyer, A.D. Friedman, R. Peto, W.R. Havender, L.S. Gold, T. Haggin, R.H. Harris, and M. Rosenfeld (1980), "Carcinogenic Potency: A Progress Report". In Banbury Report 5, "Ethylene Dichloride: A Potential Health Risk?", B. Ames, P. Infante, and R. Reitz (eds), Cold Spring Harbor Laboratory (pub), Cold Spring Harbor, New York, pp. 65 - 81.

Hooper, K., C.B. Sawyer, R. Peto, T. Haggin, A.D. Friedman, W.R. Havender, L.S. Gold, R.H. Harris, M. Rosenfeld, and B.N. Ames (1981), "Carcinogenic Potency: A Progress Report". In In Vitro Toxicity Testing of Environmental Agents, A. Kolber (ed), Plenum Press (pub), New York.

Havender, W.R. (1981), "Encounters of the Regulatory Kind", The American Spectator 14, September, pp. 25 - 26.

Havender, W.R. (1981), "The Abuse of Science in Public Policy", J. Contemporary Studies 4, September, pp. 5 - 20. Excerpted in The Wilson Quarterly VI, Spring, 1982, pp. 13 - 14.

Havender, W.R. (1981), "Politicians Make Bad Scientists", Regulation 5, November/December, pp. 46 - 48.

Havender, W.R. and E.M. Whelan (1982), "Cancer and Its Uncertainties", Cato Journal 2, Fall, pp. 543 - 564.

Ames, B.N., L.S. Gold, W.R. Havender, N.K. Hooper, and C.B. Sawyer (1982), "Carcinogenic Potency", California Policy Seminar Final Report, Institute of Governmental Studies, University of California, Berkeley, CA.

Ames, B.N., L.S. Gold, C.B. Sawyer, and W.R. Havender (1982), "Carcinogenic Potency". In Environmental Mutagens and Carcinogens (Proceedings of the Third International Conference of Environmental Mutagens), T. Sugimura, S. Kondo, and H. Takebe (eds). Published jointly by the University of Tokyo Press, Tokyo, Japan, and Alan R. Liss, Inc., New York, NY. 663 - 670.

Havender, W.R. (1983), The Science and Politics of Cyclamate", The Public Interest, No. 71, Spring, pp. 17 - 32.

Havender, W.R. (1983), "Science and Politics in Regulatory Washington", The American Spectator 16, June, pp. 23 - 26.

Havender, W.R. (1983), "The Myth of the Apolitical EPA", ACSH News & Views.4, May/June, pp. 1 ff.

Havender, W.R. (1983), "The Two-Faced Nature of Nature", ACSH News & Views 4, November/December, pp. 1 - 2.

Whelan, E.M. and W.R. Havender (1984), "Sweet Truth: What Do Scientists Really Know About Saccharin? And What Does It Mean for the Regulators" (adapted from a talk prepared for a symposium sponsored by Consumers Union held in Washington, D.C. on May 23, 1984 on the topic, "Ethical Issues and Value Conflicts in Food Safety Decision-Making"), Reason 16, October, pp. 33 - 38.

Gold,L.S., C.B. Sawyer, N.K. Hooper, W.R. Havender, and B.N. Ames (1984), "Carcinogenic Potency and the TD_{50}: Presentation of the Database", Environmental Health Perspectives (in press).

Havender, W.R. (1984), "EDB and the Marigold Option", Regulation 8, January/February, pp. 13 - 17.

Havender, W.R. (1984), "Cancer Scare of the Month: EDB", The American Spectator 17, June, pp. 29 - 31.

Havender, W.R., Op - Ed articles in The Wall Street Journal (November 3, 1983; September 4, 1984), The Los Angeles Times (Sunday, May 6, 1984), and USA Today (January 16, 1984).

Havender, W.R., Book Reviews for Fortune, The American Spectator, Regulation, Reason, and ACSH News & Views.

Selected Publications - Books:

Havender, W.R., contributor to Social Regulation: Strategies for Reform, E. Bardach and R. Kagan (eds), Institute for Contemporary Studies (pub), San Francisco, Ch. 2.(1982).

Havender, W.R., contributor to Readings in Public Policy, A. Lawrence Chickering (ed), Institute for Contemporary Studies (pub), San Francisco, Ch. 4 (1984)

Havender, W.R., contributor to Arthur Jensen: Consensus and Controversy, S. Modgil and C. Modgil (eds), Falmer Press (pub), England, forthcoming.

Havender, W.R., editor, "...It's What You Do Know That Ain't So", Heritage Foundation (pub), Washington, D.C., forthcoming.

Invited Media Appearances:

CBS Morning News (January 12, 1984)

MacNeil/Lehrer Show (January 23, 1984)

Nightline (January (February 2, 1984)

A multitude of local radio and TV shows over the past few years in New York City, Washington, D.C., Los Angeles, San Francisco, Dallas/Fort Worth, Pittsburgh, Miami, Denver, Atlanta, Seattle, Sacramento, Hartford, Providence, Oklahoma City, and Winston-Salem.